

10/657,910

<http://www.cas.org/legal/infopolicy.html>

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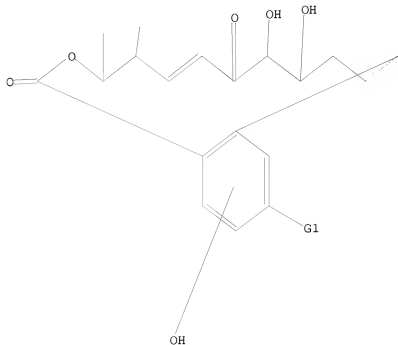
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L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR



G1 O,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...

Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 13:48:06 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 61911 TO ITERATE

Toh

20/06/2008

10/923,271

100.0% PROCESSED 61911 ITERATIONS
SEARCH TIME: 00.00.01

35 ANSWERS

L2 35 SEA SSS FUL L1

L3 2 L2

=> d 1-2 ibib abs hitstr

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on SIN

ACCESSION NUMBER: 2004:964817 CAPLUS

DOCUMENT NUMBER: 141:410756

TITLE: Preparation of macrocyclic compounds for the treatment of inflammation and autoimmune disorders

INVENTOR(S): Chiba, Kenichi; Du, Hong; Eguchi, Yoshihito; Fujita, Masanori; Goto, Masaki; Gusovsky, Fabian; Harmange, Jean-Christophe; Inoue, Atsushi; Kawada, Megumi; Kawai, Takatoshi; Kawakami, Yoshiyuki; Kimura, Akifumi; Kotake, Makoto; Kuboi, Yoshikazu; Matsushima, Tomohiro; Mizui, Yoshiharu; Muramoto, Kenzo; Sakurai, Hideki; Shen, Yong-chun; Shirota, Hiroshi; Spyvee, Mark; Tanaka, Isao; Wang, John; Wood, Ray; Yamamoto, Satoshi; Yoneda, Naoki

PATENT ASSIGNEE(S): Japan

SOURCE: U.S. Pat. Appl. Publ., 299 pp., Cont.-in-part of Appl. No. PCT/US03/07377.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040224936	A1	20041111	US 2003-657910	20030909
WO 2003076424	A1	20030918	WO 2003-US7377	20030307
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
WO 2005023792	A2	20050317	WO 2004-US29196	20040909
WO 2005023792	A3	20050623		
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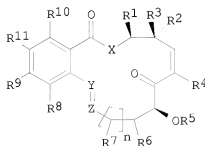
PRIORITY APPLN. INFO.:

US 2002-362883P P 20020308
 US 2002-380711P P 20020514
 WO 2003-US7377 A2 20030307
 US 2003-657910 A 20030909

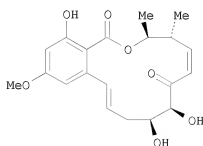
OTHER SOURCE(S):

CASREACT 141:410756; MARPAT 141:410756

GI



I



II

AB Macrocylic compds. of formula I [R1 = H, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, etc.; R2, R3 = H, halo, (substituted) OH, alkyl, aryl, etc.; R1R2, R1R3 = alkylene; R4 = H, halo; R5 = H, protecting group, prodrug; R6, R7, R11 = H, (substituted) OH; R8, R9 = H, halo, (substituted) OH, alkoxy, etc.; R10 = H, (substituted) OH, (substituted) NH2; n = 0-2; X = absent, O, NH, N-alkyl, CH2, S; Y, Z = CH, O, CO, NH, etc.] are prepared for the treatment of various disorders including inflammatory or autoimmune disorders, and disorders involving malignancy or increased angiogenesis. In certain embodiments, methods for the treatment of various disorders including inflammatory or autoimmune disorders comprise systemically (e.g., orally) administering to a subject in need thereof a therapeutically effective amount of a compound of formula I. Thus, II was prepared in several steps. Some of the compds. inhibited NF- κ B with IC50 values < 10 μ M.

IT 603039-45-8P 603045-38-1P 603045-40-5P
 603045-42-7P 603045-44-9P 603045-46-1P
 603151-24-2P 603151-32-2P 603151-34-4P
 603959-45-1P 603985-37-1P 603985-63-3P
 603985-65-5P 603985-69-9P 603985-71-3P
 603985-72-4P 603985-73-5P 603985-74-6P
 603985-75-7P 603985-77-9P 603985-78-0P
 603986-04-5P 603987-34-4P 603987-35-5P
 603987-75-3P 603987-93-5P 603988-36-9P
 791101-13-8P 791101-14-9P 791101-15-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of macrocylic compds. for the treatment of inflammatory or

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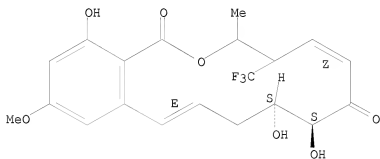
autoimmune disorders)

RN 603039-45-8 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3-methyl-4-(trifluoromethyl)-, (5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

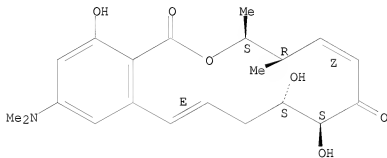


RN 603045-38-1 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(dimethylamino)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

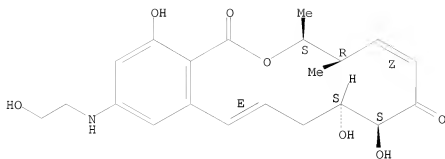


RN 603045-40-5 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[(2-hydroxyethyl)amino]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

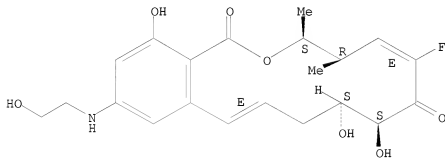


RN 603045-42-7 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[(2-hydroxyethyl)amino]-3,4-dimethyl-, (3S,4R,5E,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

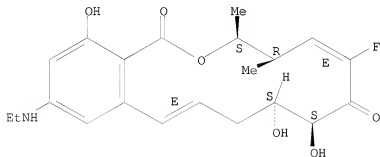


RN 603045-44-9 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(ethylamino)-6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5E,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

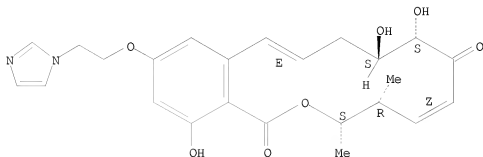
Double bond geometry as shown.



RN 603045-46-1 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[2-(1H-imidazol-1-yl)ethoxy]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

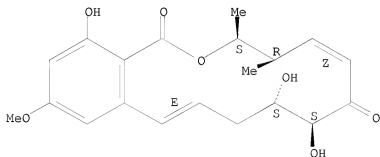
Absolute stereochemistry.
Double bond geometry as shown.



RN 603151-24-2 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

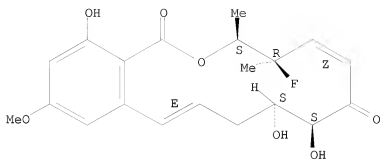
Absolute stereochemistry.
Double bond geometry as shown.



RN 603151-32-2 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 4-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

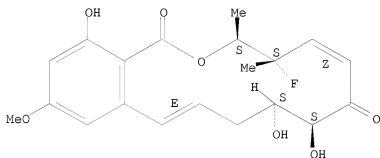


RN 603151-34-4 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 4-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3,4-dimethyl-, (3S,4S,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

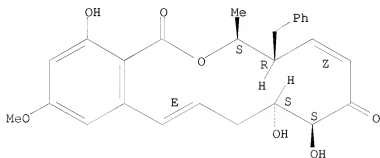


RN 603959-45-1 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3-methyl-4-(phenylmethyl)-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

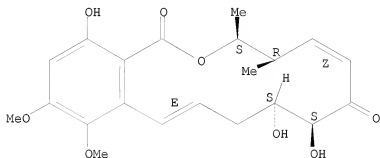


RN 603985-37-1 CAPLUS

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CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-13,14-dimethoxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

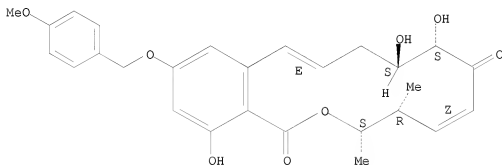
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-63-3 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[(4-methoxyphenyl)methoxyl]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

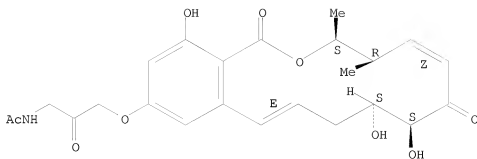
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-65-5 CAPLUS

CN Acetamide, N-[3-[[[(3S,4R,5Z,8S,9S,11E)-3,4,7,8,9,10-hexahydro-8,9,16-trihydroxy-3,4-dimethyl-1,7-dioxo-1H-2-benzoxacyclotetradecin-14-yl]oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

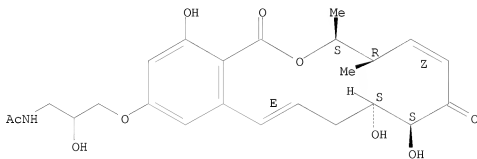


RN 603985-69-9 CAPLUS

CN Acetamide, N-[3-[[(3S,4R,5Z,8S,9S,11E)-3,4,7,8,9,10-hexahydro-8,9,16-trihydroxy-3,4-dimethyl-1,7-dioxo-1H-2-benzoxacyclotetradecin-14-yl]oxy]-2-hydroxypropyl]- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

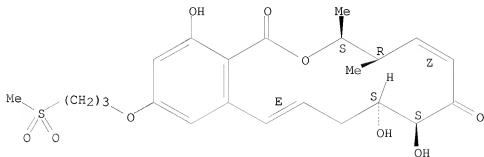


RN 603985-71-3 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-[3-(methylsulfonyl)propoxy]-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

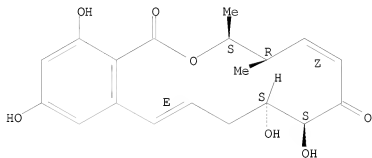


RN 603985-72-4 CAPLUS

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CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,14,16-tetrahydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

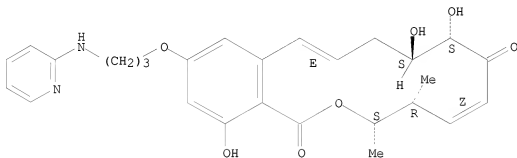
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-73-5 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-[3-(2-pyridinylamino)propoxy]-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

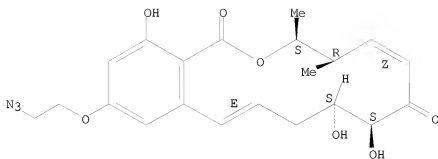
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-74-6 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(2-azidoethoxy)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

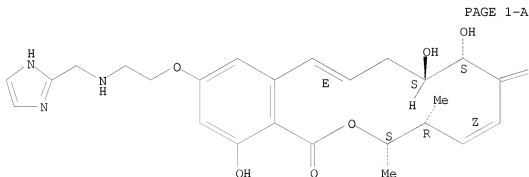
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-75-7 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[2-[(1H-imidazol-2-ylmethyl)amino]ethoxy]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



PAGE 1-A

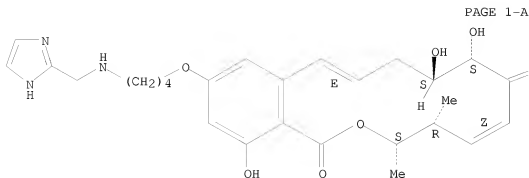
PAGE 1-B

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RN 603985-77-9 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[4-[(1H-imidazol-2-ylmethyl)amino]butoxy]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



PAGE 1-B

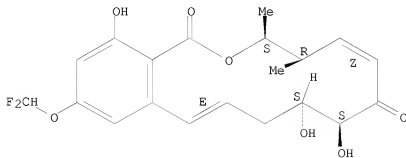
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CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(difluoromethoxy)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



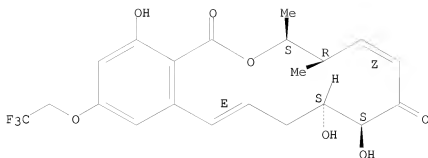
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CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-(2,2,2-trifluoroethoxy)-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

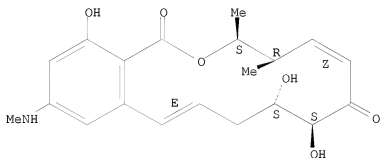
10/923,271



RN 603987-34-4 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-(methylamino)-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

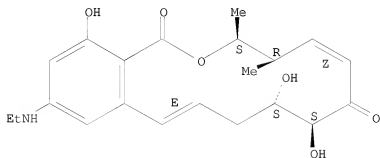
Absolute stereochemistry.
Double bond geometry as shown.



RN 603987-35-5 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(ethylamino)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

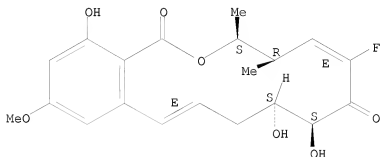


RN 603987-75-3 CAPLUS

10/923,271

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3,4-dimethyl-, (3S,4R,5E,8S,9S,11E)- (CA INDEX NAME)

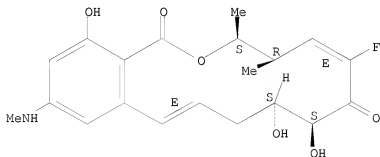
Absolute stereochemistry.
Double bond geometry as shown.



RN 603987-93-5 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-(methylamino)-, (3S,4R,5E,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

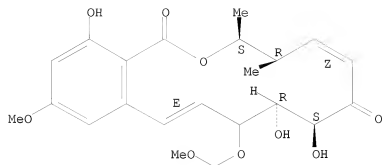


RN 603988-36-9 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-10-(methoxymethoxy)-3,4-dimethyl-, (3S,4R,5Z,8S,9R,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

10/923,271

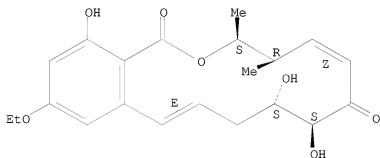


RN 791101-13-8 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-ethoxy-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

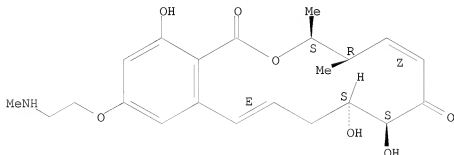


RN 791101-14-9 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-[2-(methylamino)ethoxy]-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

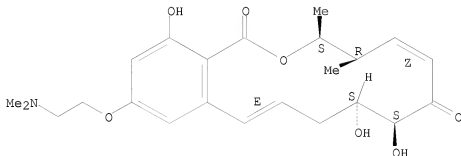
Double bond geometry as shown.



RN 791101-15-0 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-[2-(dimethylamino)ethoxy]-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)-(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:737744 CAPLUS

DOCUMENT NUMBER: 139:261090

TITLE: Preparation of macrocyclic compounds for use in pharmaceutical and cosmetic compositions which regulate various genes involved in immune and inflammatory responses

INVENTOR(S): Boivin, Roch; Chiba, Kenichi; Davis, Heather A.; Diepitro, Lucian; Du, Hong; Eguchi, Yoshihito; Fujita, Masanori; Gilbert, Sandra; Goto, Masaki; Harmange, Jean Christophe; Inoue, Atsushi; Jiang, Yimin; Kawada, Megumi; Kawai, Takatoshi; Kawakami, Yoshiyuki; Kimura, Akifumi; Kotake, Makoto; Kuboi, Yoshikazu; Lemelin, Charles; Li, Xiang-yi; Matsushima, Tomohiro; Mizui, Yoshiharu; Sakurai, Hideki; Schiller, Shawn; Shen, Yongchun; Spyvee, Mark; Tanaka, Isao; Wang, Yuan; Yamamoto, Satoshi; Yoneda, Naoki; Kobayashi, Seiichi

PATENT ASSIGNEE(S): Eisai Co. Ltd., Japan; et al.

SOURCE: PCT Int. Appl., 438 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

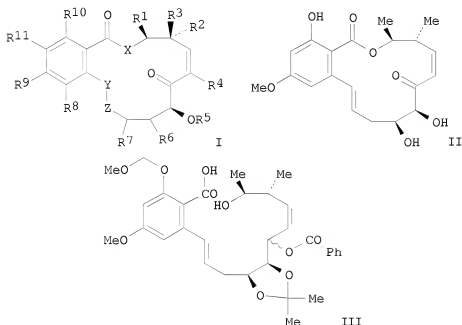
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076424	A1	20030918	WO 2003-US7377	20030307
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,			

	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG		
CA 2478065	A1	20030918	CA 2003-2478065 20030307
AU 2003224672	A1	20030922	AU 2003-224672 20030307
BR 2003008113	A	20050209	BR 2003-8113 20030307
EP 1507773	A1	20050223	EP 2003-721353 20030307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK		
JP 2005519954	T	20050707	JP 2003-574642 20030307
CN 1653059	A	20050810	CN 2003-810248 20030307
NZ 535101	A	20070727	NZ 2003-535101 20030307
US 20040224936	A1	20041111	US 2003-657910 20030909
IN 2004KN01270	A	20060714	IN 2004-KN1270 20040830
MX 2004PA08722	A	20050713	MX 2004-PA8722 20040908
NO 2004004256	A	20041207	NO 2004-4256 20041007
US 20060247448	A1	20061102	US 2004-507067 20041110
PRIORITY APPLN. INFO.:			US 2002-362883P P 20020308
			US 2002-380711P P 20020514
			WO 2003-US7377 W 20030307

OTHER SOURCE(S): MARPAT 139:261090
GI



AB Macrocyclic lactones and lactams, such as I [R1 = H, alkyl, heteroalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl; R2, R3 = H, OH, halogen, protected hydroxyl, alkyl, heteroalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl; R1R2 or R1R3 = 3-8 membered alicyclic ring; R4 = H, halogen;

R5 = H, hydroxyl protecting group, linked prodrug; R6, R7 = H, OH, protected hydroxyl; R8, R9, R10, R11 = H, OH, NH2, alkoxy, alkylamino, etc.; X = O, NH, S, CH2, etc.; R8R9 = fused ring, such as furan or imidazole; Y-Z = CH:CH, NHCO, etc.], were prepared for a variety of therapeutic and cosmetic uses, such as antitumor and anti-inflammatory agents and treatment of skin photodamage. These macrocycles are claimed for use as NF- κ B, AP-1, protein kinase, cancer cell proliferation and solid tumor angiogenesis inhibitors and for use in the treatment of inflammation, cancer, psoriasis, skin photodamage, restenosis as stent coatings, rheumatoid arthritis, asthma, sepsis, inflammatory bowel disease, atopic dermatitis, Crohn's disease, autoimmune disorders and for treatment of gastrointestinal, esophageal, tracheal/bronchial, urethral and vascular obstructions wherein the lumen of a body passageway is expanded. Thus, macrocyclic lactone II, designated as ER 803064, was prepared via a multistep synthetic sequence with included a macrolactonization reaction of III to form the desired lactone ring. The prepared macrocycles were assayed for their effect on TNF- α and β -actin placental alkaline phosphatase transcription using human acute monocytic leukemia cells.

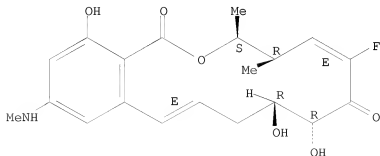
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 603985-37-1P 603985-63-3P 603985-64-4P
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 804606 603985-72-4P 603985-73-5P 603985-74-6P
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 603987-34-4P 603987-35-5P 603987-75-3P
 603987-93-5P, ER 806821 603988-36-9P

RL: COS (Cosmetic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of macrocyclic compds. for use in pharmaceutical and cosmetic compns. which regulate various genes involved in immune and inflammatory responses)

RN 603044-46-8 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-(methylamino)-, (3S,4R,5E,8R,9R,11E)-(CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



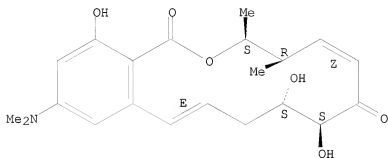
10/923,271

RN 603045-38-1 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(dimethylamino)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

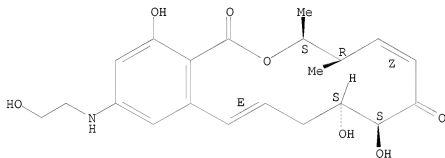


RN 603045-40-5 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[(2-hydroxyethyl)amino]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

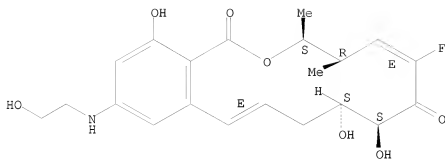


RN 603045-42-7 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[(2-hydroxyethyl)amino]-3,4-dimethyl-, (3S,4R,5E,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

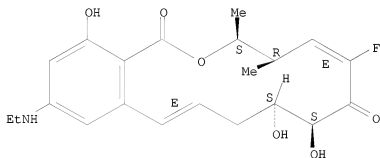
Double bond geometry as shown.



RN 603045-44-9 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(ethylamino)-6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5E,8S,9S,11E)- (CA INDEX NAME)

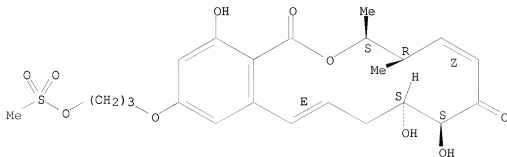
Absolute stereochemistry.
Double bond geometry as shown.



RN 603045-45-0 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-[3-[(methylsulfonyl)oxy]propoxy]-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

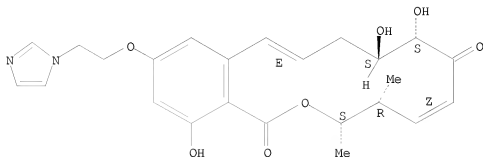


RN 603045-46-1 CAPLUS

10/923,271

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[2-(1H-imidazol-1-yl)ethoxy]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

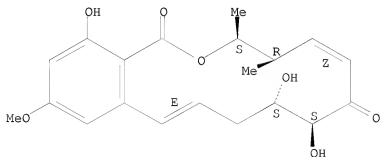
Absolute stereochemistry.
Double bond geometry as shown.



RN 603151-24-2 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

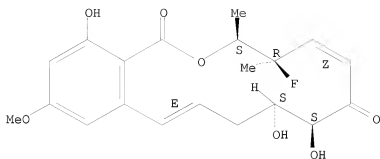
Absolute stereochemistry.
Double bond geometry as shown.



RN 603151-32-2 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 4-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

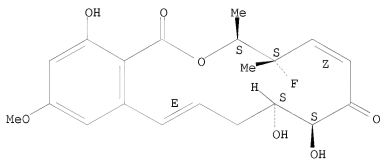
Absolute stereochemistry.
Double bond geometry as shown.



RN 603151-34-4 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 4-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3,4-dimethyl-, (3S,4S,5Z,8S,9S,11E)- (CA INDEX NAME)

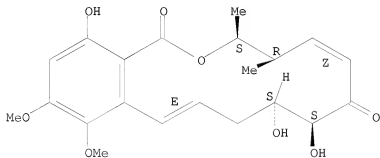
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-37-1 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-13,14-dimethoxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

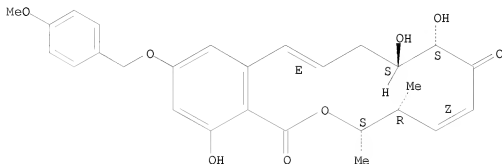


RN 603985-63-3 CAPLUS

10/923,271

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[(4-methoxyphenyl)methoxy]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

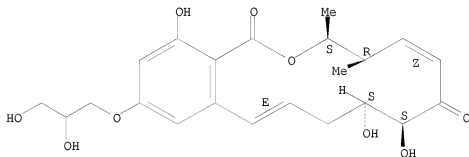
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-64-4 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(2,3-dihydroxypropoxy)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

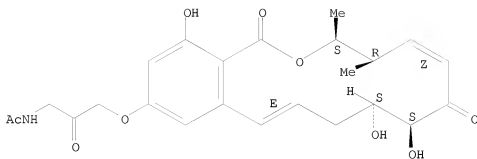
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-65-5 CAPLUS

CN Acetamide, N-[3-[[[(3S,4R,5Z,8S,9S,11E)-3,4,7,8,9,10-hexahydro-8,9,16-trihydroxy-3,4-dimethyl-1,7-dioxo-1H-2-benzoxacyclotetradecin-14-yl]oxy]-2-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

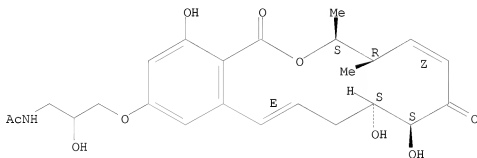


RN 603985-69-9 CAPLUS

CN Acetamide, N-[3-[[(3S, 4R, 5Z, 8S, 9S, 11E)-3, 4, 7, 8, 9, 10-hexahydro-8, 9, 16-trihydroxy-3, 4-dimethyl-1, 7-dioxo-1H-2-benzoxacyclotetradecin-14-yl]oxy]-2-hydroxypropyl]- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

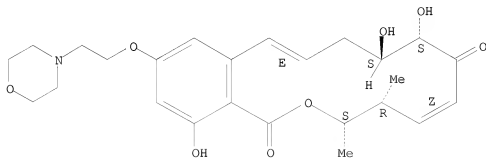


RN 603985-70-2 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1, 7 (8H)-dione, 3, 4, 9, 10-tetrahydro-8, 9, 16-trihydroxy-3, 4-dimethyl-14-[2-(4-morpholinyl)ethoxy]-, (3S, 4R, 5Z, 8S, 9S, 11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

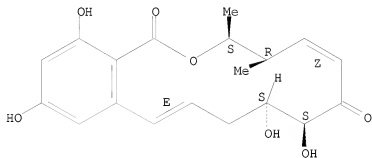


RN 603985-72-4 CAPLUS

10/923,271

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,14,16-tetrahydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

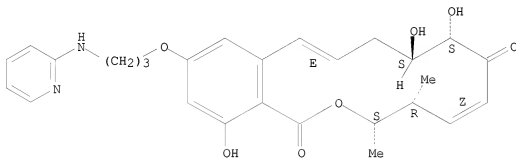
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-73-5 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-[3-(2-pyridinylamino)propoxy]-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

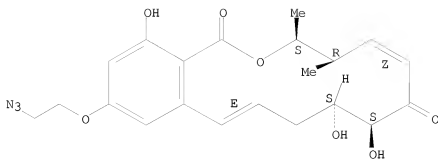
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-74-6 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(2-azidoethoxy)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

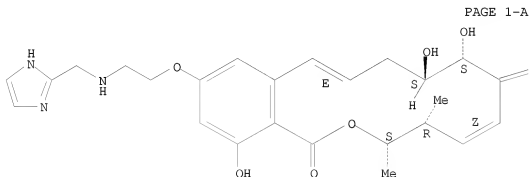
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-75-7 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[2-[(1H-imidazol-2-ylmethyl)amino]ethoxy]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



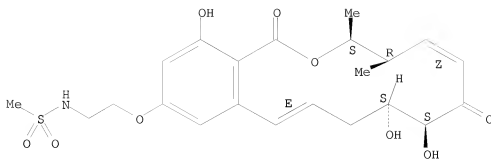
PAGE 1-B

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RN 603985-76-8 CAPLUS

CN Methanesulfonamide, N-[2-[[[(3S,4R,5Z,8S,9S,11E)-3,4,7,8,9,10-hexahydro-8,9,16-trihydroxy-3,4-dimethyl-1,7-dioxo-1H-2-benzoxacyclotetradecin-14-yl]oxy]ethyl]- (CA INDEX NAME)

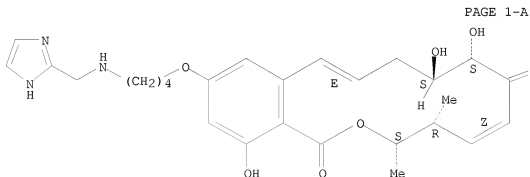
Absolute stereochemistry.
Double bond geometry as shown.



RN 603985-77-9 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-[(1H-imidazol-2-ylmethyl)amino]butoxy]-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



PAGE 1-A

PAGE 1-B

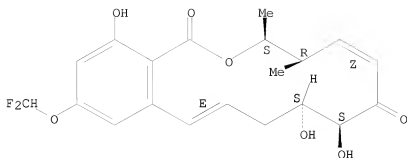
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RN 603985-78-0 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(difluoromethoxy)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

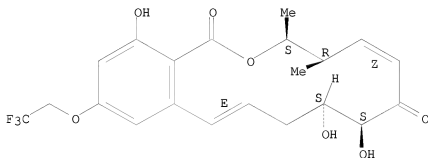
10/923,271



RN 603986-04-5 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-(2,2,2-trifluoroethoxy)-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

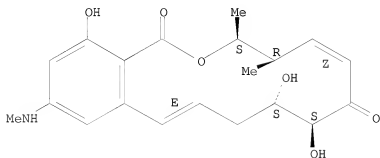
Absolute stereochemistry.
Double bond geometry as shown.



RN 603987-34-4 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-(methylamino)-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

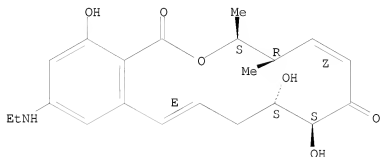


RN 603987-35-5 CAPLUS

10/923,271

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 14-(ethylamino)-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

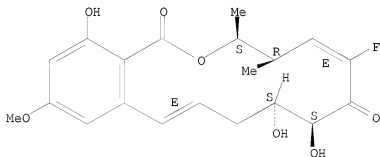
Absolute stereochemistry.
Double bond geometry as shown.



RN 603987-75-3 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3,4-dimethyl-, (3S,4R,5E,8S,9S,11E)- (CA INDEX NAME)

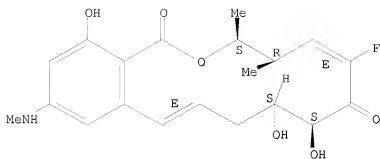
Absolute stereochemistry.
Double bond geometry as shown.



RN 603987-93-5 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 6-fluoro-3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-(methylamino)-, (3S,4R,5E,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

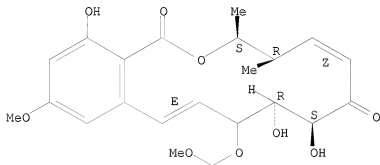


RN 603988-36-9 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-10-(methoxymethoxy)-3,4-dimethyl-, (3S,4R,5Z,8S,9R,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 603039-45-8P 603959-45-1P 603985-71-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

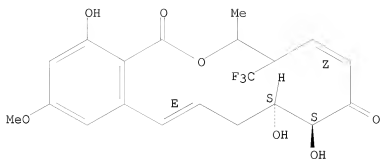
(preparation of macrocyclic compds. for use in pharmaceutical and cosmetic compns. which regulate various genes involved in immune and inflammatory responses)

RN 603039-45-8 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3-methyl-4-(trifluoromethyl)-, (5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

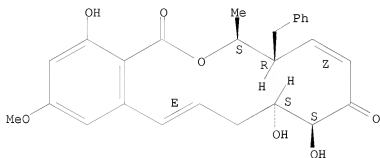


RN 603959-45-1 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-14-methoxy-3-methyl-4-(phenylmethyl)-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

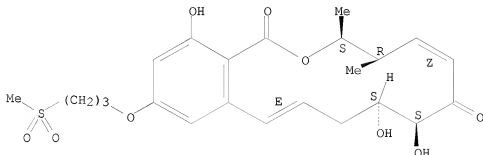


RN 603985-71-3 CAPLUS

CN 1H-2-Benzoxacyclotetradecin-1,7(8H)-dione, 3,4,9,10-tetrahydro-8,9,16-trihydroxy-3,4-dimethyl-14-[3-(methylsulfonyl)propoxy]-, (3S,4R,5Z,8S,9S,11E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

10/923,271

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT